

**FAX**

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**DATE:** February 3, 1998

**TO:**

Examiner Stephanie Zitomer  
Group Art Unit 1807  
U.S. Patent and Trademark Office

**FROM:**

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**NUMBER OF PAGES INCLUDING THIS COVER: 7**

**Applicant:** STEPHEN P. A. FODOR et al

**Serial No.** 08/670,118


**Filed:** June 25, 1996

**For:** A METHOD OF DETECTING NUCLEIC ACIDS

Examiner Zitomer,

Enclosed is a Supplemental Response for filing in the above-identified application..  
Please call with any concerns.

Regards,

  
Nancy J. DeSantis  
Attorney for Applicant

rev. 8/94

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2/3/98

**OFFICIAL****IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of: \_\_\_\_\_ )

STEPHEN P. A. FODOR et al \_\_\_\_\_ )

Serial No. 08/670,118 \_\_\_\_\_ )

Filed: June 25, 1996 \_\_\_\_\_ )

For: A METHOD OF DETECTING  
NUCLEIC ACIDS \_\_\_\_\_ )

Examiner: Zitomer

Art Unit: 1807

SUPPLEMENTAL AMENDMENT  
AND RESPONSECOMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

Sir:

In supplemental response to the Office Action dated September 3, 1997, Applicants request consideration of the amendments and remarks set forth below. This supplemental response addresses the topics discussed by the Examiner and Applicants' representative, Paul Kokulis, by telephone on or about January 15, 1998.

**IN THE CLAIMS**

Please cancel claims 26-31 without prejudice to further prosecution in a related application. Cancellation of these claims does not constitute abandonment of any subject matter.

Claim 32, line 11, after the phrase "comprising a sequence" in (b) (ii), insert the word  
-- substantially --.

**REMARKS**

Claims 26-34, 38, and 39 are currently pending. Claims 26-31 are canceled for prosecution in a related application, and to expedite prosecution of this application.. Applicants noted an inconsistency in wording in Claim 32 that has been corrected.

**A. Rejections under 35 U.S.C. Section 103**

Claims 32-34 stand rejected over WO 89/10977 ("Southern") in view of U.S. Patent No. 5,445,934 ("Fodor") and in further view of U.S. Patent No. 5,215, 882 ("Bahl") and, in further view of U.S. Patent No. 4,855,225 (Fung). Claims 26-31 stand rejected as unpatentable over Southern in view of Fodor. A double patenting rejection was also applied to Claims 26-31. Even assuming for the sake of argument only that the references can be cited against the pending claims, a prima facie case of obviousness has not been established.

**1. Claims 32-34**

First, there is no motivation to combine the cited references: Southern in view of Fodor in further view of Bahl in further view of Fung. Second, even if combined, the combination of the references fails to suggest the claimed invention.

Southern alone or in combination does not render the claims obvious. Claim

32 recites detecting the nucleic acid sequences in two or more collections of nucleic acid molecules using labels that are distinguishable from each other in the same assay.

Specifically, the claims recites:

32. A method for detecting nucleic acid sequences in two or more collections of nucleic acid molecules, the method comprising:

- (a) providing an array of polynucleotides bound to a solid surface, each said polynucleotide comprising a determinable nucleic acid;
- (b) contacting the array of polynucleotides with:
  - (i) a first collection of labeled nucleic acid comprising a sequence substantially complementary to a nucleic acid of said array; and
  - (ii) at least a second collection of labeled nucleic acid comprising a sequence complementary to a nucleic acid of said array;

wherein the first and second labels are distinguishable from each other; and

- (c) detecting hybridization of the first and second labeled complementary nucleic acids to nucleic acids of said arrays.

The Office Action recognizes that Southern does not suggest using distinguishable labels as claimed. Instead, Southern repeatedly discusses using autoradiography, which does not suggest the use of multiple and distinguishable labels. See, for example, Southern at page 9, line 11; page 13, line 18; page 16, lines 20-32; page 17, lines 18-21; page 18, lines 31-32; page 19, line 30; page 21, line 5; and page 27, line 23. In passing, Southern briefly notes that autoradiography has limitations in resolution and that “some direct detection system would be better.” Southern at page 14, lines 9-13. Southern then mentions fluorescent probes and speculates that “the low sensitivity of fluorescence may not be a problem.” Southern at page 14, lines 13-16. Even here, the Southern reference at

best notes that another single-label system may be more useful than autoradiography.

Accordingly, Southern teaches directly away from Applicants' claims.

Regarding Fodor, there is no motivation to combine Fodor's pioneering work with Southern. Further, the Office Action recognizes that the combination of Fodor and Southern does not provide the distinguishable labels claimed. Bahl does not remedy these defects -- Bahl does not suggest distinguishable labels in the recited assay. At column 5, lines 23-39 (the citation provided by the Office Action), Bahl discusses having different targets in different stripes, which does not suggest using distinguishable labels in a single assay. Applicants note that Bahl's discussion at Col 6, line 28 - Col 7, line 15, of various labeling methods does not suggest that any of those labels should or could be used in a single system so as to be distinguishable from one another. Therefore Bahl also teaches away from the claims, which recite "wherein the first and second label are distinguishable from each other." There is nothing to motivate one skilled in the art to combine Southern in view of Fodor in further view of Bahl, and the combination once made fails to establish what is claimed.

The combination of Southern in view of Fodor in further view of Bahl in further view of Fung also fails to establish obviousness. The references provide no motivation to make the cited combination. Fung, like Southern and Bahl, teaches away from the claimed subject matter. Fung is cited as teaching "differentially labeled probes." Office Action at page 7. Fung, however, discusses using labels to detect nucleic acids separated electrophoretically in a gel. Unlike Fung, claim 32 recites providing an array of immobilized nucleic acids, contacting the array with at least two collections of polynucleotides having distinguishable labels, and detecting the hybridization of the labeled polynucleotides with the nucleic acids of the array. The present claims involve detection of nucleic acids bound together via complementary hybridization in a single assay with multiple

distinguishable labels. Thus the combination including Fung not only fails to suggest the claimed invention, it teaches away from what is claimed. For at least these reasons, a prima facie case of obviousness has not been established for claims 32-34.

## 2. Claims 26-31

Claims 26-31 stand rejected as obvious over Southern in view of Fodor. A double patenting rejection was also made to these claims. These claims are canceled without prejudice to further prosecution to expedite prosecution of this application.

## B. OTHER MATTERS

Applicants wish to point out that a related patent to the Southern reference (WO 89/10977) was issued recently as a U.S. Patent (5,700,637). It is not believed that this patent has bearing on the discussion herein, but is brought to the Examiner's attention for the sake of completeness.

**CONCLUSION**

In view of the foregoing remarks and the amendment to the claims, it is believed that all claims are now in condition for allowance. Hence, it is respectfully requested that the application be passed to issue at an early date. If for any reason the Examiner feels that a telephone conference would in any way expedite prosecution of the subject application, the Examiner is invited to telephone the undersigned at 408-731-5000.

Respectfully submitted,  
AFFYMETRIX, INC.

Date: 2/3/98

By: 

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